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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/019,192	06/20/2002	Kattesh V. Katti	0994.00133	6247

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EXAMINER	
KRASS, FREDERICK F	

ART UNIT	PAPER NUMBER
1614	9

DATE MAILED: 07/30/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Offic Action Summary	Application No. 10/019,192	Applicant(s) KATTI ET AL.	
	Examiner Frederick Krass	Art Unit 1614	

-- Th MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-7 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-7 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on 6-20-02 is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 8 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

Scope of Enablement Rejection

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 5-7 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the treatment of two specific types of digestive tract carcinomas (colon and gastric), does not reasonably provide enablement for the treatment of all cancers generally, nor the "prevention" of metastasis in any particular type of cancer, nor "arresting" cell growth in any particular cell type. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Attention is directed to In re Wands, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing Ex parte Forman, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

1) the quantity of experimentation necessary,
2) the amount of direction or guidance provided,
3) the presence or absence of working examples,
4) the nature of the invention,
5) the state of the prior art,
6) the relative skill of those in the art,
7) the predictability of the art, and
8) the breadth of the claims.

The instant specification fails to provide guidance that would allow the skilled artisan to practice the instant invention without resorting to undue experimentation, as discussed in the subsections set forth hereinbelow.

1. The nature of the invention, state of the prior art, relative skill of those in the art, and the predictability of the art

The claimed invention relates to chemotherapy, and the relative skill of those in the art is high, generally that of a PHD or MD.

A. Treatment by Cancer Type

While the state of the art is relatively high with regard to the treatment of specific cancers with specific agents, it has long been underdeveloped with regard to the treatment of cancers broadly. In particular, there is no known anticancer agent which is effective against all cancers. This is why the National Cancer Institute (NCI) has the extensive *in vitro* drug screening program it does. As discussed by the court in In re Brana, 34 U.S.P.Q.2d 1436, 51 F.3d 1560 (1995), *in vitro* assays are used by NCI (such as the P388 and L1210 lymphocytic leukemia tests at issue therein) to measure the potential antitumor properties of a candidate compound. Brana at 1562-63. If success is shown in this initial screening step, this demonstrates that at least one cancer type (e.g., lymphocytic leukemia) is sensitive thereto, and provides the incentive to select it for

further studies to determine its usefulness as a chemotherapeutic agent against other cancer types (lung, breast, colon, etc.) Id. at 1567-68. These *in vitro* tests are then considered reasonably correlative of success *in vivo*.

Thus, a considerable amount of *in vitro* empirical testing is required, with no *a priori* expectation of success being present, before a candidate anticancer agent can be considered useful against any particular cancer type.

B. "Prevention" or "Cure"

It is well-known in the art that the "prevention" or "cure" of cancer is highly unpredictable, and indeed is generally not even practical. As discussed by U.S. Patent 5,416,091 at col. 1, lines 22-38:

> Complete cures of various tumors like leukemias, lymphomas and solid tumors by the use of chemotherapeutic agents are rare because of the heterogeneous sensitivity of tumor cells to each antitumor agent. Cancer chemotherapy also fails because of intrinsic resistance of tumors to multiple drug therapies. In other cases, a tumor may become may become resistant to the antitumor agents used in a previous treatment. The therapeutic effects of these agents are then eliminated. An even graver problem is that recurrent cancers are resistant not only the cancer suppressants used in previous treatments, but also manifest resistance to other antitumor agents, unrelated to the agent used previously either by chemical structure or mechanism of action. These phenomenon are collectively referred to a multiple drug resistance (mdr) and contributed widely to cancer treatment failures in the clinic.

2. The breadth of the claims

The claims are very broad and inclusive of 1) the treatment of any type of cancer (claim 5); 2) the "prevention" of metastasis in any type of cancer (claim 6) and 3) "arresting cell growth" in any cell type (claim 7).

3. The amount of direction or guidance provided and the presence or absence of working examples

The specification provides specific direction only for the treatment of colon and gastric carcinomas by inhibiting their growth (see page 13 of the instant specification; speculation about treating other cancer types is made at page 17, but no data confirming success is provided). No other cancer types are tested, and no evidence of "prevention" of metastasis or "arresting" cell growth is provided.

4. The quantity of experimentation necessary

The lack of adequate guidance from the specification or prior art with regard to the actual treatment of all cancers in a mammal with the claimed compounds fails to rebut the presumption of unpredictability extant in this art. Applicants fail to provide the guidance and information required to ascertain which particular type of cancer the claimed anticancer agent will be effective against without resorting to undue experimentation. Applicant's limited disclosure of several specific cancers is noted but is not sufficient to justify claiming all cancers broadly.

Absent a reasonable *a priori* expectation of success for using a specific gold/hydroxyalkylphosphine complex to treat any particular type of cancer, one skilled in the art would have to extensively test many various complexes against many different cancer types. Since each prospective embodiment, and indeed future embodiments as the art progresses, would have to be empirically tested, and those which initially failed tested further, an undue amount of experimentation would be required to practice the invention as its is claimed in its current scope, because the specification provides inadequate guidance to do otherwise.

Similarly, the instant specification provides no guidance whatsoever for achieving the extremely rare therapeutic condition of "prevention" of metastasis or "arresting cell growth" (the functional equivalent of "cure").

Obviousness Rejection

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Katti et al (USP 5,843,993) in view of Fricker ("Medicinal chemistry and pharmacology of gold compounds", *Transition Met. Chem.*, vol. 21, 377-383 (1996)).

The primary reference discloses hydroxyalkylphosphine-gold complexes, and fairly suggests their use as cancer chemotherapeutic agents (col. 1, lines 35-45, for example). Additional therapeutic agents may be administered therewith (col. 6, lines 37 et seq.) The prior art differs from the instant claims insofar as it does not exemplify, *ipsissima verba*, complexes containing non-radioactive gold. While it uses the term "gold" broadly, the exemplified and preferred embodiments all use radioactive species. It is noted, however, that the reference broadly suggests both diagnostic (where radioactive labeling would be indicated) as well as therapeutic applications (where radioactivity would not be indicated). See for example col. 7, lines 26 et seq. (with the treatment of arthritis being taught at line 27). Note also that the invention is characterized by patentees at col. 1, lines 14 and 15 as relating to "pharmaceutical, *especially* radiopharmaceuticals", which implies the use of non-radioactive pharmaceuticals as a less preferred embodiment.

It is well-known to use gold complexes in non-radioactive form for various types of therapies, particularly the treatment of arthritis, but also in treating cancer as well. See the secondary reference at pp. 378-79, which is cited to demonstrate the state of the art. The prior art differs from the instant claims insofar as it is silent regarding hydroxyalkylphosphine ligands.

It would have been obvious to have administered non-radioactive gold-hydroxyalkylphosphine complexes when treating arthritis as suggested by the secondary reference, since such administration is well-known as illustrated by the

secondary reference. Additional motivation for avoiding the use of radioactive products to avoid unnecessary health and environmental risks would be self-evident as well.

Obviousness-Type Double Patenting Rejection

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-4 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-8 of U.S. Patent No. 5,843,993 taken in view of Fricker ("Medicinal chemistry and pharmacology of gold compounds", *Transition Met. Chem.*, vol. 21, 377-383 (1996)).

The instant claims are drawn to non-radioactive gold-hydroxyalkylphosphine complexes. That subject matter differs from the conflicting claims of the patent only insofar as the latter recites the equivalent radioactive gold complexes. Note that claim 1 of the patent uses the preamble "for use as a diagnostic or therapeutic pharmaceutical". Accordingly, it would have been obvious to have modified the conflicting complexes to

incorporate non-radioactive gold for the same reasons detailed in the rejection set forth in the "Obviousness Rejection" supra.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frederick Krass whose telephone number is (703) 308-4335. The examiner can normally be reached on Monday, Tuesday and Thursday from 9am to 5pm, and on Friday from 11am to 7pm. The examiner is off Wednesday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marianne Seidel, can be reached at (703) 308-4725. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0193.

Frederick Krass
Primary Examiner
Art Unit 1614